

# REMARKS

This Preliminary Amendment is being filed concurrently with Applicant's Rule 53(b) continuation application.

A clean copy of now pending claims 26 and 46-60 is provided above. A clean copy of the amendments to the specification is also provided above.

The specification has been amended to reflect the correct priority application information and the current address of the ATCC depository. The specification, namely, the Brief Description of the Drawings, has also been amended to reflect the numbering of certain formal drawings which are being filed herewith.

Claims 1-25 and 27-45 have been canceled without prejudice. Independent claim 26 as originally filed in the parent application remains pending. Claims 46-60 have been added. These added claims are fully supported by the specification (see, e.g., pages 44-49, 62, and 71-74), and do not introduce new matter.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attachment is captioned "Version with markings to show changes made."

Respectfully submitted,  
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PATENT TRADEMARK OFFICE

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the specification:**

In the paragraph beginning at line 10 of page 1, the text has been amended as follows:

--- [This is a non-provisional application claiming] This application is a continuation application of Serial Number 08/829,270 filed March 31, 1997, which claims priority under 35 USC 119(e) to provisional application numbers 60/014,699 filed April 1, 1996, now abandoned, and 60/026,943 filed September 23, 1996, now abandoned, the contents of which are incorporated herein by reference. -

In the paragraph on page 11, lines 16-18, the text has been amended as follows:

---Figures 2A-2B show[s] an alignment of the amino acid sequence encoded by clone 18.1 of Apo-2LI with extracellular regions of other members of the human TNF receptor family.---

In the paragraph on page 11, lines 22-28, the text has been amended as follows:

---Figures 4A-4C show[s] the nucleotide sequence of native sequence human Apo-3 cDNA and its derived amino acid sequence. The putative signal sequence and transmembrane domain are underlined, the death domain sequence is boxed, and the potential N-linked glycosylation sites are marked with an asterisk. Also boxed is the alanine residue which was present in the fetal lung but not in the fetal heart cDNA clone (discussed in Example 4 below).---

In the paragraph on page 54, lines 24-34 - page 55, line 1, the text has been amended as follows:

---Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected

Serial No.: not yet assigned

antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, [Rockville, Maryland] Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63].---

In the paragraph on page 64, lines 4-11, the text has been amended as follows:

---All restriction enzymes referred to in the examples were purchased from New England Biolabs and used according to manufacturer's instructions. All other commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, [Rockville, Maryland] Manassas, Virginia.

In the paragraph on page 77, lines 3-5, the text has been amended as follows:

---The following materials have been deposited with the American Type Culture Collection, [12301 Parklawn Drive, Rockville, MD] 10801 University Blvd., Manassas, Virginia, USA (ATCC): ---

**In the claims:**

Please cancel claims 1-25 and 27-45 without prejudice.

Please add the following claims:

-46. A method of blocking or inhibiting Apo-3 receptor, comprising

Serial No.: not yet assigned

exposing mammalian cells expressing Apo-3 receptor to an effective amount of anti-Apo-3 antibody, wherein said antibody (a) comprises an antigen binding site which binds to an Apo-3 receptor polypeptide comprising amino acid residues 1 to 417 of SEQ ID NO:6 or an extracellular domain sequence of Apo-3 receptor polypeptide which comprises amino acid residues 25 to 198 of SEQ ID NO:6 and (b) blocks or inhibits Apo-3 receptor induced apoptosis in said mammalian cells or Apo-3 receptor activation of NF-kB in said mammalian cells.

47. The method of claim 46 wherein said anti-Apo-3 antibody is a chimeric antibody.

48. The method of claim 46 wherein said anti-Apo-3 antibody is a humanized antibody.

49. The method of claim 46 wherein said anti-Apo-3 antibody is a human antibody.

50. The method of claim 46 wherein said anti-Apo-3 antibody is a monovalent antibody.

51. The method of claim 50 wherein said monovalent antibody is a Fab fragment.

52. The method of claim 46 wherein said anti-Apo-3 antibody is labeled with a detectable moiety capable of directly or indirectly producing a signal.

53. The method of claim 52 wherein said detectable moiety is a radioisotope, fluorescent compound or chemiluminescent compound.

54. The method of claim 46 wherein said mammalian cells are exposed to said anti-Apo-3 antibody *in vivo*.

Serial No.: not yet assigned

55. The method of claim 46 wherein said anti-Apo-3 antibody blocks or inhibits Apo-3 receptor induced apoptosis in said mammalian cells.

56. A method of blocking or inhibiting Apo-3 receptor, comprising exposing mammalian cells expressing Apo-3 receptor to an effective amount of Apo-3 receptor immunoadhesin, wherein said immunoadhesin (a) comprises an Apo-3 receptor polypeptide comprising amino acid residues 1 to 417 of SEQ ID NO:6 or a fragment thereof and (b) blocks or inhibits Apo-3 receptor induced apoptosis in said mammalian cells or Apo-3 receptor activation of NF-kB in said mammalian cells.

57. The method of claim 56 wherein said Apo-3 receptor immunoadhesin comprises an immunoglobulin constant region.

58. The method of claim 56 wherein said fragment of the Apo-3 receptor polypeptide comprises amino acid residues 1 to 198 of SEQ ID NO:6.

59. The method of claim 56 wherein said Apo-3 receptor immunoadhesin blocks or inhibits Apo-3 receptor induced apoptosis in said mammalian cells.

60. The method of claim 56 wherein said mammalian cells are exposed to said Apo-3 receptor immunoadhesin *in vivo*. ---